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Syntheses of sugar-related trihydroxyazepanes from simple carbohydrates and their activities as reversible glycosidase inhibitors

Søren M. Andersen [a], Christian Ekhart [b], Inge Lundt [a,*], Arnold E. Stütz [b]

[a] *Department of Organic Chemistry, Technical University of Denmark, Building 201, DK-2800 Lyngby, Denmark*
[b] *Institut für Organische Chemie der Technischen Universität Graz, Stremayrgasse 16, A-8010 Graz, Austria*

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Abstract

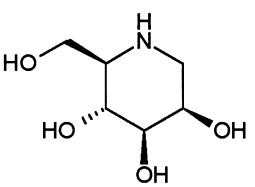
Five diastereomeric trideoxy-1,6-iminohexitols were synthesised, and their inhibitory activities were determined against selected glycosidases. For comparison, 1,4,5-trideoxy-1,5-imino-D-*lyxo*-hexitol, the 4-deoxy derivative of 1-deoxymannojirimicin, was prepared by enzymatic isomerisation of 6-azido-3,6-dideoxy-D-*ribo*-hexose into the corresponding 2-ulose and subsequent hydrogenation accompanied by intramolecular reductive amination.

Keywords: Trihydroxy azepanes; Glycosidase inhibitors; Simple carbohydrates

1. Introduction

Several sugar analogues with basic nitrogen instead of oxygen in the ring (imino sugars) have been discovered as natural products, and have attracted considerable attention due to their pronounced glycosidase inhibitory properties leading to notable biological effects [1].

Many D-mannosidases as well as known α-L-fucosidases are strongly inhibited by such imino sugars and imino alditols structurally related to their natural substrates. 1-Deoxymannojirimycin (**1**) and the bicyclic alkaloid swainsonine (**2**) are good mannosidase inhibitors, and 1-deoxyfuconojirimycin (**3**) is the most powerful inhibitor of α-L-fucosidases known to date; thus these are important tools for glycobiology.



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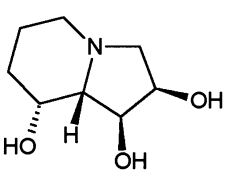

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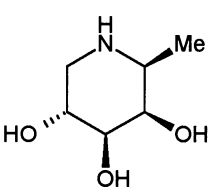

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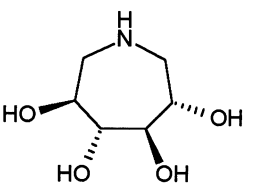

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Due to the similarity of the D-mannosyl and the L-fucosyl moieties, good D-mannosidase inhibitors frequently also inhibit α-L-fucosidases and vice versa. Hence, with respect to their potentially interesting properties as tools

* Corresponding author. Tel.: +45-45-252133; fax: +45-45-933968.
E-mail address: okil@pop.dtu.dk (I. Lundt)

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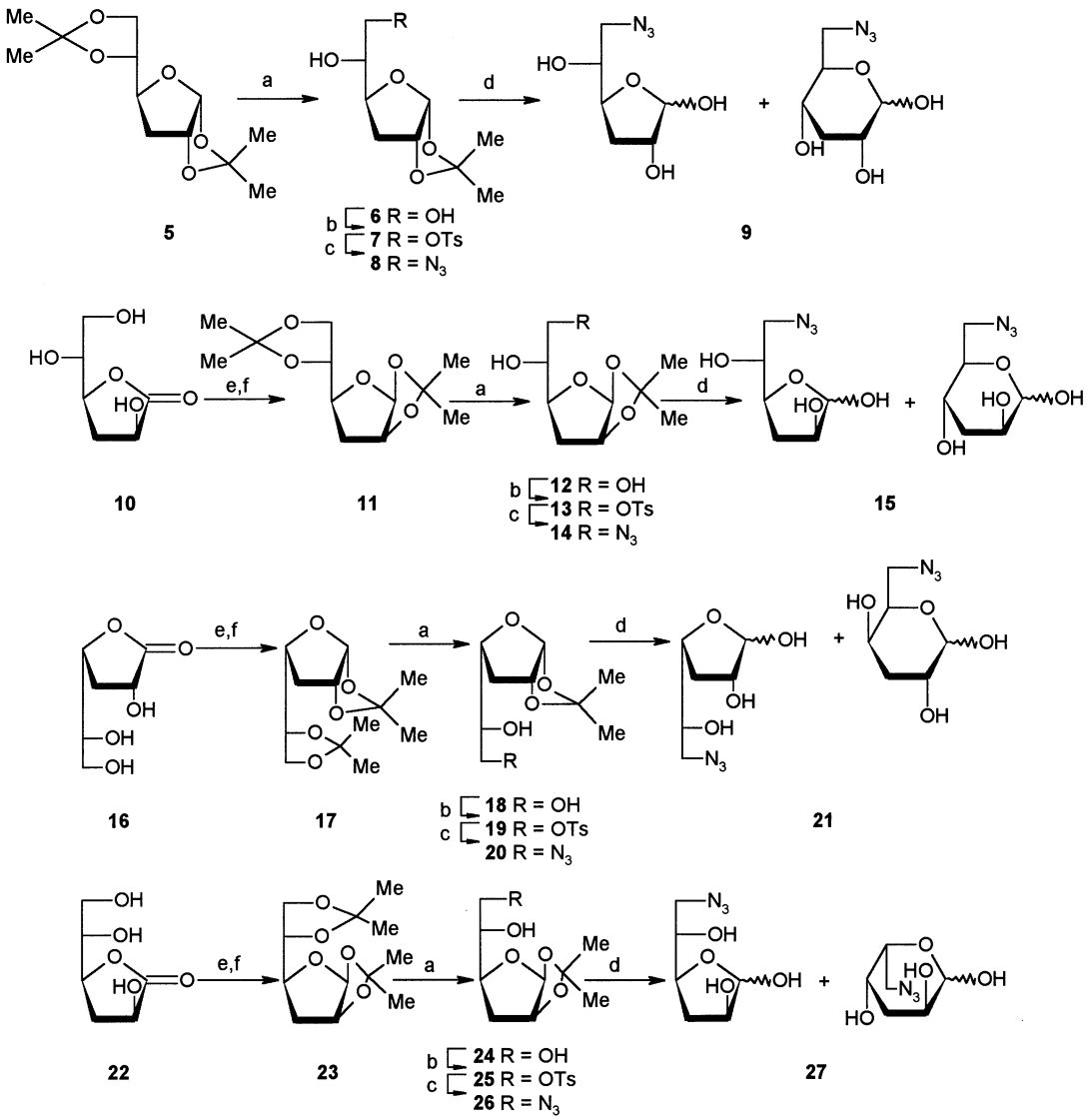
in glycobiology and glycotechnology, selective inhibitors of either L-fucosidases or D-mannosidases have been deemed highly desirable. Basic structure–activity relationships in the area of mannosidase inhibitors have been discussed in important work by Winkler and Holan with the aid of computer-assisted molecular modelling [2]. For example, these workers correlated hydroxyl groups in the powerful mannosidase inhibitor swainsonine with hydroxyl groups at C-2, C-3, and C-6 in 1-deoxymannojirimycin. Despite their efforts, quite a few activity-determining structural requirements, such as conformational prerequisites and the number and positions of hydroxyl groups necessary for a good inhibitor, have remained not fully understood. In context with our continuing interest in the synthesis and biological evaluation of novel selective inhibitors of D-mannosidases [3] as well as α-L-fucosidases [3–5], we became interested in seven-membered ring imino alditols as potential inhibitors of the types of enzymes under consideration. We hoped that due to the flexibility of the azepane ring system, certain conformational advantages over the five- and the six-membered ring inhibitors in terms of fitting into the active sites of glycosidases might emerge. As was suggested by molecular modelling, trihydroxyazepanes bearing one unsubstituted methylene group along the chain might be interesting for the elucidation of selectivities as well as structure–activity relationships in these systems. Recently, such a tetrahydroxyazepane (**4**) with C_2-symmetry was found by Wong and his group [6,7], as well as by Le Merrer et al. [8], to exhibit noteworthy glycosidase inhibitory properties against quite a range of different types of glycosidases.

This fact was rationalised by superpositioning the functional groups of the azepane and those of a range of proven powerful glycosidase inhibitors, which in many of the cases reported were found to match nicely [7]. Thus, we decided to synthesise two diastereomeric trihydroxyazepanes, compounds **28** and **29**, which are structurally related to the established inhibitors of D-mannosidases (**1** and **2**), as well as L-fucosidases (**1** and **3**). Furthermore, two additional epimers (compounds **30** and **31**) and a regioisomer (compound **33**) were synthesised in order to estimate the importance for biological activity of the presence and orientation of different hydroxyl groups on the ring. In addition, we wished to probe a point raised by Winkler and Holan on the minimum structural requirements of mannosidase inhibitors related to 1-deoxymannojirimycin, namely that the positions of the three hydroxyl groups in swainsonine (**2**) are related to the orientations of OH-2, OH-3, and OH-6 in 1-deoxymannojirimycin (**1**). Conveniently, both issues could be addressed by the same synthetic approach via easily available 6-azido-3,6-dideoxysugars, taking advantage of an additional enzymatic key step in the preparation of desired 1,4,5-trideoxy-1,5-imino-D-*lyxo*-hexitol (1,4-dideoxymannojirimycin, **35**).

2. Results and discussion

Synthesis.—The 6-azido-3,6-dideoxysugars can be easily prepared from partially protected 3-deoxysugars. Of these, the required 3-deoxy-D-*ribo*-hexose (**5**) is readily obtained from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose [9]. Other 1,2:5,6-protected 3-deoxyhexoses are more conveniently prepared by conventional reduction [10] of 3-deoxy-hexono-1,4-lactones [11], followed by protection of the resulting free 3-deoxyaldoses. Regioselective deprotection of O-5 and O-6 in the 1,2:5,6-di-*O*-isopropylidene protected 3-deoxyhexoses **5**, **11**, **17**, and **23**, followed by 6-*O*-sulfonylation, gave the primary tosylates **7**, **13**, **19**, and **25**, respectively. Subsequent displacement with azide led to the corresponding 6-azidodeoxy derivatives **8**, **14**, **20**, and **26**, which by conventional deprotection furnished the corresponding free 6-azido-3,6-dideoxyhexoses with D-*ribo* (**9**), D-*arabino* (**15**), D-*xylo* (**21**), and L-*xylo* (**27**) configurations, respectively, in good yields (Scheme 1).

Catalytic reduction using hydrogen in the presence of palladium-on-charcoal (5%) and concomitant intramolecular reductive amination of the intermediary 6-aminodeoxy sugars led to the desired 2,4,5-trihydroxyazepanes **28**–**31** (Scheme 2). The 3,4,5-trihydroxyazepane **33**, a regioisomer of **29** with D-*ara*-



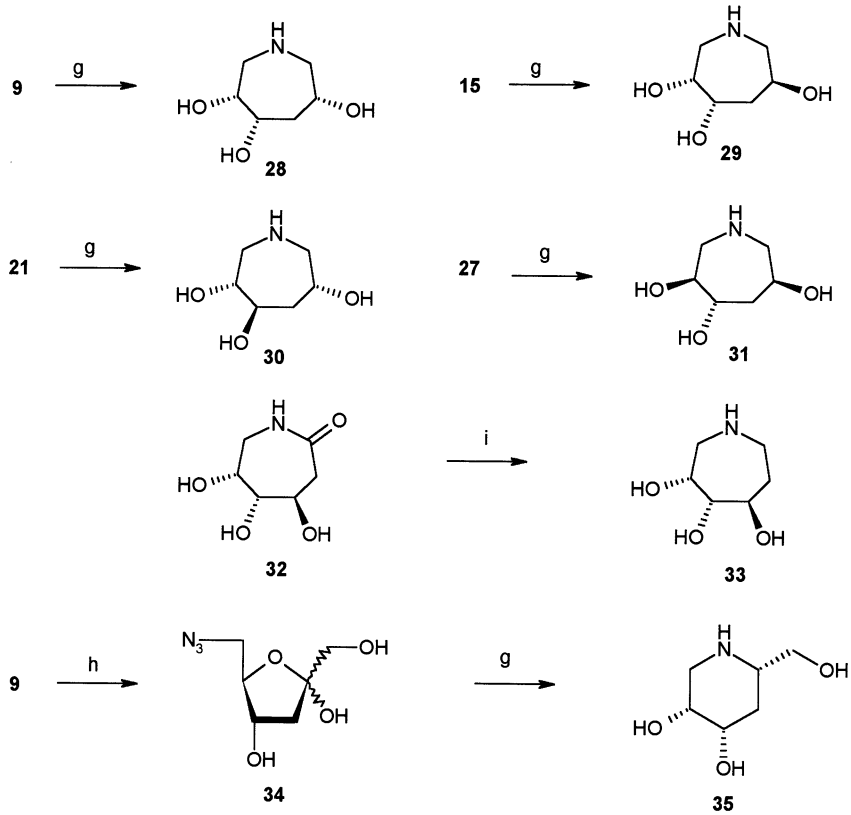
Scheme 1. (a) 90% AcOH (aq). (b) Tosyl chloride, pyridine. (c) NaN_3, DMF, reflux 1 h. (d) Amberlite IR-120 (H^+), H_2O–CH_3CN, 40 °C. (e) Disiamylborane, THF. (f) Acetone, camphor sulfonic acid (cat).

bino configuration, was prepared by reduction of the lactam **32**, readily obtainable from 2,6-dibromo-2,6-dideoxy-D-mannolactone [12].

Following previous studies [13] and preliminary experiments [14] on the tolerance of an immobilised glucose isomerase (Sweetzyme T from Novo Nordisk A/S) for non-natural substrate analogues, the azidodideoxyhexoses obtained were exposed to this enzyme. Gratifyingly, azidodideoxysugar **9** could be converted into the 6-azido-3,6-dideoxy derivative of D-fructofuranose **34** in more than 70% isolated yield. Conversely, azidodideoxyhexoses **15**, **21**, and **27** did not give conversion rates with glucose isomerase that were significantly different from results of control experiments in the absence of the enzyme under the slightly basic conditions employed in this study. Catalytic reduction of the ketose **34** furnished 1,4,5-trideoxy-1,5-imino-D-*lyxo*-hexitol (1,4-dideoxymannojirimycin, **35**) in good yield and with high diastereoselectivity.

Inhibition of glycosidases.—Activities of **28**, **29**, **30**, **31**, **33** and **35** were determined with a variety of glycosidases, and the results are listed in Table 1.

Trihydroxyazepanes **28**–**31** did not exhibit any appreciable inhibitory activity against the glycosidases employed in this study. Apart from the lack of symmetry as compared with active azepanes such as **4**, the spatial distribution of functional groups in the preferred con-



Scheme 2. (g) 5% Pd/C, H_2, MeOH. (h) Glucose isomerase, H_2O–CH_3CN, 60 °C. (i) $BH_3 \cdot Me_2S$.

Table 1
Inhibition of glycosidases with compounds **28**, **29**, **30**, **31**, **33**, and **35**

Enzymes	K_i (μM) [a]					
	28	**29**	**30**	**31**	**33**	**35**
α-D-Glucosidase (baker's yeast)	142	NI	NI	NI	13	12
β-D-Glucosidase (almond)	72	NI	200	NI	NI	51
α-D-Galactosidase (green coffee bean)	NI	NI	NI	NI	78	NI
α-D-Galactosidase (*Escherichia coli*)	NI	NI	NI	NI	27	13
α-D-Mannosidase (jack bean)	NI	NI	314	NI	140	NI
β-D-Mannosidase (snail acetone powder)	NI	NI	NI	NI	150	196
β-*N*-Acetylglucosaminidase (jack bean)	107	112	72	76	196	156
α-L-Fucosidase (bovine kidney)	800	NI	<b306.			

[a] NI: $K_i > 1$ mM.

formations neither match the motifs of substrates, nor those of proven inhibitors or proposed transition states such as the putative 'flap-up' mannopyranosyl oxocarbonium ion. The comparably good values found with azepane **33** can be attributed to the fact that this compound can adopt conformations that superimpose to varying degrees with established glycosidase inhibitors. Superposition of azepane **33** with the glucosidase inhibitor 1-deoxynojirimycin shows good alignment of the secondary hydroxyl groups of both molecules. The selectivity of **33** for α-glucosidases can be related to the lack of a hydroxyl group matching OH-6 of 1-deoxynojirimycin, as it has been found that α-glucosidases, as opposed to their β-specific counterparts, do not require this structural feature for recogni-

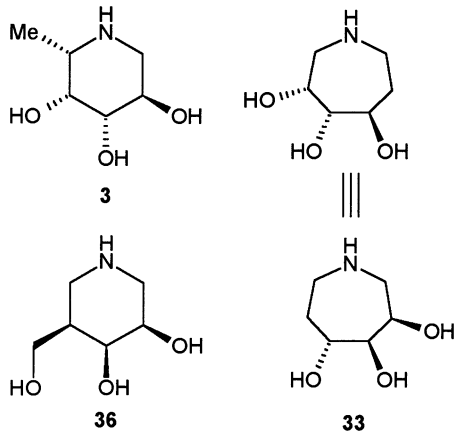


Fig. 1. Comparison of the spatial characteristics among 1-deoxyfuconojirimycin (**3**), 4-epi-isofagomine (**36**) and trihydroxyazepane **33**.

tion/binding [15]. Galactosidase inhibitory action was found to be stronger with the β-galactosidase probed. This might be due to the fact that **33** exhibits a similar alignment of functional groups as the 4-epi analogue of isofagomine **36** ($K_i = 4$ nM with β-galactosidase from *Aspergillus oryzae* at pH 6.8) (Fig. 1) [16]. Mannosidase inhibitory activity of **33** was found in the same range for both the α- and the β-specific enzyme probed. A comparison of Dreiding models and computer-aided superposition with the 'flap-up' mannopyranosyl oxocarbocation ion (Fig. 2) shows excellent matching of hydroxyl groups with 2-OH, 3-OH, as well as 4-OH of the latter, but a distinct deviation of the position of the ring nitrogen. This and the lack of a hydroxy group in the position of OH-6 seem to be responsible for the lower activity as compared with good inhibitors of D-mannosidases such as 1-deoxymannojirimycin (**1**). The α-L-fucosidase inhibitory activity exhibited by **33** was expected, since the compound has the minimal structural motif necessary for inhibition of this enzyme [5]. The inhibition can then most likely be attributed to the good fitting of the ring nitrogen as well as all three hydroxyl groups with the L-fucose/1-deoxy-L-fuconojirimycin (**3**) structural motif (Fig. 1).

As with 1,5-dideoxy-1,5-imino-D-arabinitol ($K_i = 40$ μM at pH 5 with the enzyme from bovine kidney) [4], the *nor* derivative of the powerful inhibitor 1,5-dideoxy-1,5-imino-L-fucitol (**3**), the lack of the methyl group at C-5, which was found to be a vital prerequisite for pronounced inhibition, is limiting this particular activity. In Fig. 3 the superposition of 1,5-dideoxy-1,5-imino-D-arabinitol with **33** is shown.

The reasons for the activities found with the 4-deoxy derivative of 1-deoxymannojirimycin (**35**) with glycosidases are not apparent. Its selective β-galactosidase inhibitory activity seems noteworthy.

In conclusion, the most active compounds in this study, azepane **33** and piperidine **35**, were found to be more effective against D-glucosidases and D-galactosidases than against the other enzymes probed. This points to the

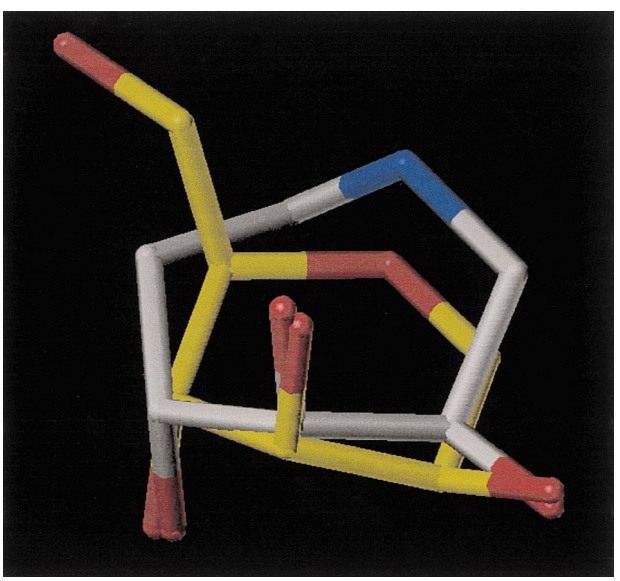


Fig. 2. Superposition of mannopyranosyl oxocarbonium ion with compound **33**.

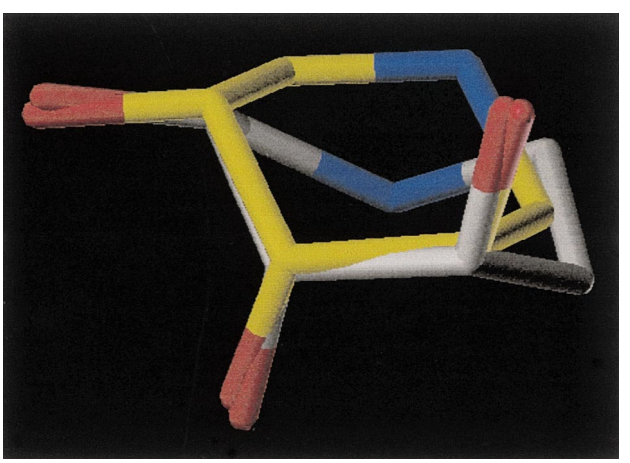


Fig. 3. Superposition of 1,5-dideoxy-1,5-imino-D-arabinitol with compound **33**.

fact that in the azepane series, three vicinal hydroxyl groups appear to be essential for basic glycosidase inhibitory activity. In the case of piperidine **35**, deoxygenation at C-4 and, consequently, improved flexibility provide an interesting shift from selectivity for D-mannosidases and α-L-fucosidase found with the parent compound **1** to activity against D-glucosidase and β-D-galactosidase.

3. Experimental

General methods.—^{1}H and ^{13}C NMR spectra were obtained on Bruker instruments AC 200, AC 250 and AM 500. Chemical shifts are reported in δ (ppm), and coupling constants are given in Hz. For NMR spectra in $CDCl_3$, the chloroform signal was used as reference for ^{1}H NMR spectra (7.27 ppm) and ^{13}C NMR spectra (77.0 ppm). For NMR spectra in MeOH-d_4, the MeOH signal was used as a reference (3.31 ppm for the ^{1}H NMR spectra and 49.0 ppm for the ^{13}C NMR spectra). Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. Microanalyses were carried out at the Institut für Physikalische Chemie der Universität Wien and the Research Institute for Pharmacy and Biochemistry, Prague. Thin-layer chromatography (TLC) was performed on E. Merck Silica Gel 60 F_{254} precoated plates and was visualised by spraying with a mixture of 1.5% (w/w) $NH_4Mo_7O_{24}\cdot 4\,H_2O$, 1% (w/w) $Ce(SO_4)_2\cdot 4\,H_2O$ and 10% (v/v) H_2SO_4, followed by heating. Flash chromatography was conducted on Silica Gel 60 (E. Merck, 40–63 μm and Grace AB Amicon, 35–70 μm). Evaporations were performed in vacuo at temperatures below 45 °C. All solvents were distilled before use. The calculations were performed using Sybyl 6.5 on an Octane workstation by Silicon Graphics. Calculations/modelling were carried out as follows: (1) charges were derived by the Gasteiger–Hückel method; (2) the minimiser was set to terminate after 10,000 steps or energy convergency; (3) the BGFS-minimiser was used; (4) the dielectric constant was set to 4; (5) the Tripos Force Field was employed, and (6) the molecules were minimised after sketching. Simulated annealing, for 2000 fs at 600 K, and then cooling down for 10,000 fs to 50 K in 10 separate cycles, minimised before annealing, and cooled in a logarithmic function. The best four candidates were discriminated by the lowest potential energy after minimisation and clustering of the simulated annealing sampled conformations.

General procedures

*Regioselective removal of the 5,6-*O*-isopropylidene group*. The 3-deoxy-1,2:5,6-di-*O*-isopropylidenehexofuranose (1 g) was stirred at ambient temperature in 90% aq AcOH (10 mL). The reaction was followed by TLC. When the reaction was complete (6–10 h), the solution was neutralised and concentrated.

Regioselective tosylation. To a solution of 3-deoxy-1,2-*O*-isopropylidenehexofuranose (1 g) in pyridine (20 mL), tosyl chloride (1.2 equiv) was added at 0 °C. The mixture was stirred at ambient temperature for 16 h. Ice was added, and the reaction mixture was concentrated to a residue that was dissolved in CH_2Cl_2 (30 mL). The organic phase was washed consecutively with 4 M HCl (10 mL) and satd aq $NaHCO_3$ (10 mL), dried ($MgSO_4$), and concentrated.

Nucleophilic substitution with azide. NaN_3 (1.5 equiv) was added to a solution of 3-deoxy-6-*O*-tosyl-1,2-*O*-isopropylidenehexofuranose (1 g) in *N*,*N*-dimethylformamide (10 mL). The mixture was held at reflux for 1 h with protection from light. The mixture was then concentrated, and partitioned between diethyl ether (40 mL) and water (10 mL). The organic phase was washed with water (10 mL), treated with activated carbon, dried ($MgSO_4$), and concentrated.

*Removal of the 1,2-*O*-isopropylidene group*. To a solution of the 6-azido-3,6-dideoxy-1,2-*O*-isopropylidenehexofuranose (1 g) in CH_3CN (10 mL) and water (10 mL), Amberlite IR-120 [H^+] (5 mL, wet) was added. The reaction mixture was stirred at 40 °C overnight. The ion-exchange resin was filtered off, and the filtrate was concentrated.

Reduction of lactones.—To a solution of borane–methyl sulfide complex (6 equiv) in THF (10 mL), 2-methyl-2-butene (12 equiv)

was added at 0 °C under a nitrogen atmosphere over a 10-min period. After 2.5 h at ambient temperature, the 3-deoxyhexonolactone (1 g) was added as a solid over 30 min and stirred overnight under a nitrogen atmosphere. Water (3 mL) was slowly added, and the mixture was refluxed for 4 h. The solution was concentrated and extracted with water (2×20 mL). The aqueous phase was consecutively washed with CH_2Cl_2 ($20 + 10$ mL) and diethyl ether (20 mL), and concentrated.

Di-O-*isopropylidene protection*. To a suspension of 3-deoxyhexose (1 g) and acetone (40 mL), camphorsulfonic acid (0.1 g) was added. The mixture was refluxed in a Soxhlet apparatus overnight. The solution was neutralised with $NaHCO_3$. The mixture was concentrated and partitioned between ethyl acetate (20 mL) and water (10 mL). The organic phase was washed with water (10 mL), treated with activated carbon, dried ($MgSO_4$), and concentrated.

Hydrogenation. To a solution of the hexose (200 mg) in MeOH (20 mL), a suspension of a catalytic amount of 5% Pd/C in MeOH (10 mL) (Caution! extreme fire hazard!) was added. The mixture was hydrogenated at 3 MPa and ambient temperature for 16 h. The catalyst was filtered off, and the solvent was evaporated.

*3-Deoxy-1,2-*O*-isopropylidene-α-*D*-ribo-hexofuranose* (**6**).—Regioselective deprotection of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**5**, 805 mg, 3.30 mmol), following the general procedure, gave a pale-yellow syrup (1.07 g), which after chromatography (1:1 hexane–EtOAc) afforded compound **6** (570 mg, 85%) as a syrup that crystallised slowly, mp 80–82 °C. Recrystallisation from Et_2O afforded a pure sample (322 mg, 48%), mp 81–82 °C, $[\alpha]_D$ −18.5° (*c* 1.2, $CHCl_3$). ^{1}H NMR (MeOH-d_4, 500 MHz): δ 5.78 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.8 (H-2), 4.20 (ddd, 1 H, $J_{3a,4}$ 5.0, $J_{3b,4}$ 10.5, $J_{4,5}$ 5.0 Hz, H-4), 3.70 (ddd, 1 H, $J_{5,6a}$ 4.5, $J_{5,6b}$ 6.0 Hz, H-5), 3.59 (dd, 1 H, $J_{6a,6b}$ 11.5 Hz, H-6a), 3.51 (dd, 1 H, H-6b), 2.05 (dd, 1 H, $J_{3a,3b}$ 13.5 Hz, H-3a), 1.83 (ddd, 1 H, $J_{2,3b}$ 5.0 Hz, H-3b). ^{13}C NMR (MeOH-d_4, 125.8 MHz): δ 106.9 (C-1), 81.9 and 79.9 (C-2 and C-4), 73.9 (C-5), 64.6 (C-6), 35.0 (C-3). Anal. Calcd for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 53.05; H, 8.08.

*6-Azido-3,6-dideoxy-α/β-*D*-ribo-hexose* (**9**)

*3-Deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-α-*D*-ribo-hexofuranose* (**7**). Regioselective O-tosylation of 3-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**6**) (2.77 g, 13.6 mmol), following the general procedure, gave a pale syrup (5.31 g), which after chromatography (1:1 hexane–EtOAc) yielded product **7** (3.82 g, 78%) as a syrup. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.74 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.70 (dd, 1 H, $J_{2,3b}$ 4.5 Hz, H-2), 3.9–4.2 (complex, 4 H, H-4, H-5, H-6a, H-6b), 2.06 (dd, 1 H, $J_{3a,3b}$ 13.5, $J_{3a,4}$ 4.5 Hz, H-3a), 1.76 (ddd, 1 H, $J_{3b,4}$ 10.5 Hz, H-3b). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 105.0 (C-1), 80.0 and 77.2 (C-2 and C-4), 70.8 (C-6), 69.8 (C-5), 33.8 (C-3).

*6-Azido-3,6-dideoxy-1,2-*O*-isopropylidene-α-*D*-ribo-hexofuranose* (**8**). Reaction of 3-deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-α-D-*ribo*-hexofuranose (**7**) (3.58 g, 9.99 mmol) with NaN_3 according to the general procedure gave compound **8** (1.81 g, 79%) as a pale-yellow syrup. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.79 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.75 (dd, 1 H, $J_{2,3b}$ 3.5 Hz, H-2), 4.17 (ddd, 1 H, $J_{3a,4}$ 4.5, $J_{3b,4}$ 10.5, $J_{4,5}$ 4.5 Hz, H-4), 3.96 (ddd, 1 H, $J_{5,6a}$ 4.5, $J_{5,6b}$ 6.5 Hz, H-5), 3.39 (dd, 1 H, $J_{6a,6b}$ 13.0 Hz, H-6a), 3.31 (dd, 1 H, H-6b), 2.07 (dd, 1 H, $J_{3a,3b}$ 13.5 Hz, H-3a), 1.84 (ddd, 1 H, H-3b). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 105.2 (C-1), 80.4 and 78.5 (C-2 and C-4), 70.8 (C-5), 53.2 (C-6), 33.2 (C-3).

*6-Azido-3,6-dideoxy-α/β-*D*-ribo-hexose* (**9**). 6-Azido-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**8**, 880 mg, 3.84 mmol) was hydrolysed to a yellow syrup that was purified by chromatography (EtOAc) to yield compound **9** as a semi-crystalline compound (520 mg, 71%). By addition of diethyl ether, **9** crystallised (260 mg, 36%), mp 109.5–110.5 °C, $[\alpha]_D$ +31.5° (*c* 1.1, H_2O). NMR (D_2O) showed an anomeric mixture of the furanose and pyranose forms. ^{13}C NMR (D_2O, 50.3 MHz): δ 102.6 (C-1, β-furanose), 98.7 (C-1, α-furanose), 97.3 (C-1, β-pyranose), 91.7 (C-1, α-pyranose). Anal. Calcd for $C_6H_{11}N_3O_4$: C, 38.09; H, 5.87; N, 22.21. Found: C, 38.12; H, 5.89; N, 21.96.

*3-Deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-β-*D*-arabino-hexofuranose* (**13**)

*3-Deoxy-1,2:5,6-di-*O*-isopropylidene-β-*D*-arabino-hexofuranose* (**11**). 3-Deoxy-D-*arabino*-hexono-1,4-lactone (**10**) [11] (5.66 g, 34.9 mmol) was reduced following the general procedure and subsequently protected to give **11** as a pale-yellow syrup (2.34 g, 27%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.75 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.73 (ddd, 1 H, $J_{2,3a}$ 1.5, $J_{2,3b}$ 5.5 Hz, H-2), 4.31 (ddd, 1 H, $J_{4,5}$ 9.0, $J_{5,6a}$ 5.5, $J_{5,6b}$ 5.5 Hz, H-5), 4.11 (dd, 1 H, $J_{6a,6b}$ 9.0 Hz, H-6a), 3.99 (ddd, 1 H, $J_{3a,4}$ 3.0, $J_{3b,4}$ 8.0 Hz, H-4), 3.91 (dd, 1 H, H-6b), 2.31 (ddd, 1 H, $J_{3a,3b}$ 14.5 Hz, H-3a), 2.17 (ddd, 1 H, H-3b). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 106.5 (C-1), 82.0 and 80.7 (C-2 and C-4), 77.0 (C-5), 67.8 (C-6), 33.9 (C-3).

*3-Deoxy-1,2-*O*-isopropylidene-β-*D*-arabino-hexofuranose* (**12**). Regioselective deprotection of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-β-D-*arabino*-hexofuranose (**11**, 2.02 g, 8.27 mmol) gave a crude material that was purified by chromatography (EtOAc) to furnish compound **12** as a syrup (1.13 g, 67%). ^{1}H NMR (MeOH-d_4, 250 MHz): δ 5.74 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.75 (ddd, 1 H, $J_{2,3a}$ 1.0, $J_{2,3b}$ 6.0 Hz, H-2), 3.95 (ddd, 1 H, $J_{3a,4}$ 2.5, $J_{3b,4}$ 8.0, $J_{4,5}$ 9.0 Hz, H-4), 3.82 (ddd, 1 H, $J_{5,6a}$ 3.0, $J_{5,6b}$ 6.0 Hz, H-5), 3.73 (dd, 1 H, $J_{6a,6b}$ 11.0 Hz, H-6a), 3.50 (dd, 1 H, H-6b), 2.28 (ddd, 1 H, $J_{3a,3b}$ 14.0 Hz, H-3a), 2.12 (ddd, 1 H, H-3b). ^{13}C NMR (MeOH-D_4, 62.9 MHz): δ 108.0 (C-1), 82.0 (C-2 and C-4), 74.1 (C-5), 64.8 (C-6), 34.1 (C-3).

*3-Deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-β-*D*-arabino-hexofuranose* (**13**). Regioselective O-tosylation of 3-deoxy-1,2-*O*-isopropylidene-β-D-*arabino*-hexofuranose (**12**, 467 mg, 2.29 mmol) gave a crystalline residue (602 mg, 73%). By addition of EtOAc–hexane, product **13** crystallised (353 mg, 43%), mp 98–100 °C. Recrystallisation from EtOAc–hexane gave an analytical sample: mp 101 °C, $[\alpha]_D$ + 52.5° (*c* 1.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.73 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.70 (ddd, 1 H, $J_{2,3a}$ 1.0, $J_{2,3b}$ 6.0 Hz, H-2), 4.29 (dd, 1 H, $J_{5,6a}$ 2.5, $J_{6a,6b}$ 10.0 Hz, H-6a), 4.11 (dddd, $J_{4,5}$ 8.5, $J_{5,6b}$ 6.5, $J_{5,OH}$ 5.0 Hz, H-5), 4.05 (dd, 1 H, H-6b), 4.02 (ddd, 1 H, $J_{3a,4}$ 2.5, $J_{3b,4}$ 8.5 Hz, H-4), 2.68 (d, 1 H, OH), 2.34 (ddd, 1 H, $J_{3a,3b}$ 14.5 Hz, H-3a), 2.13 (ddd, 1 H, H-3b). ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 106.4 (C-1), 80.3 and 80.0 (C-2 and C-4), 71.7 (C-6), 70.5 (C-5), 32.6 (C-3). Anal. Calcd for $C_{16}H_{22}O_7S$: C, 53.62; H, 6.19. Found: C, 53.61; H, 6.22.

*6-Azido-3,6-dideoxy-1,2-*O*-isopropylidene-β-*D*-arabino-hexofuranose* (**14**).—Reaction of 3-deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-β-D-*arabino*-hexofuranose (**13**, 870 mg, 2.43 mmol) with NaN_3 furnished a crystalline residue (450 mg, 81%), which by addition of pentane gave crystalline compound **14** (202 mg, 36%), mp 67–68 °C. Recrystallisation from pentane afforded an analytical sample: mp 67–68 °C, $[\alpha]_D$ + 31.6° (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.78 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.75 (ddd, 1 H, $J_{2,3a}$ 1.0, $J_{2,3b}$ 6.0 Hz, H-2), 4.05 (complex, 2 H, H-4, H-5), 3.59 (dd, 1 H, $J_{5,6a}$ 3.0, $J_{6a,6b}$ 12.5 Hz, H-6a), 3.42 (dd, 1 H, $J_{5,6b}$ 6.0 Hz, H-6b), 2.46 (d, 1 H, $J_{OH,5}$ 4.5 Hz, OH), 2.34 (broad d, 1 H, $J_{3a,3b}$ 14.5 Hz, H-3a), 2.17 (ddd, 1 H, $J_{3b,4}$ 8.0 Hz, H-3b). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 106.4 (C-1), 81.2 and 80.5 (C-2 and C-4), 71.7 (C-5), 54.2 (C-6), 32.7 (C-3). Anal. Calcd for $C_6H_{15}N_3O_4$: C, 47.15; H, 6.60; N, 18.33. Found: C, 47.17; H, 6.49; N, 18.06.

*6-Azido-3,6-dideoxy-α,β-*D*-arabino-hexose* (**15**).—Deprotection of 6-azido-3,6-dideoxy-1,2-*O*-isopropylidene-β-D-*arabino*-hexofuranose (**14**, 430 mg, 1.88 mmol) gave a crude product (243 mg, 68%) that was purified by chromatography (EtOAc) to give free sugar **15** as a syrup (222 mg, 62%). NMR (D_2O) showed an anomeric mixture of furanose and pyranose forms. ^{13}C NMR (D_2O, 50.3 MHz): δ 104.4 (C-1, β-furanose), 97.7 (C-1, α-furanose), 97.2 (C-1, β-pyranose), 96.1 (C-1, α-pyranose).

*3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-*D*-xylo-hexofuranose* (**17**). Following the general procedure, 3-deoxy-D-*xylo*-hexono-1,4-lactone (**16**, 5.19 g, 32.0 mmol) was converted into crude crystalline compound **17** (3.49 g, 44%). By addition of hexane, **17** crystallised (2.17 g, 27%), mp 71–76 °C. Several recrystallisations from hexane afforded an analytical sample: mp 76–78 °C, $[\alpha]_D$ −29.5° (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 5.78 (d, 1 H, $J_{1,2}$

4.0 Hz, H-1), 4.70 (broad dd, 1 H, $J_{2,3a}$ 5.0 Hz, H-2), 4.41 (ddd, 1 H, $J_{4,5}$ 8.5, $J_{5,6a}$ 7.0, $J_{5,6b}$ 7.0 Hz, H-5), 4.08 (ddd, 1 H, $J_{3a,4}$ 8.5, $J_{3b,4}$ 3.5 Hz, H-4), 4.02 (dd, 1 H, $J_{6a,6b}$ 8.0 Hz, H-6a), 3.58 (dd, 1 H, H-6b), 2.19 (ddd, 1 H, $J_{3a,3b}$ 14.5 Hz, H-3a), 1.79 (broad dd, 1 H, H-3b). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 106.3 (C-1), 81.4 and 80.3 (C-2 and C-4), 77.5 (C-5), 65.9 (C-6), 33.4 (C-3). Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.26. Found: C, 58.76; H, 8.20.

*3-Deoxy-1,2-*O*-isopropylidene-α-*D*-xylo-hexofuranose* (**18**). Regioselective deprotection of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*xylo*-hexofuranose (**17**, 5.50 g, 22.5 mmol) gave a yellow syrup (5.6 g). Purification by chromatography (EtOAc) yielded product **18** (2.20 g, 48%) as a syrup, which crystallised upon addition of EtOAc–Et_2O to give pure material (1.30 g, 28%), mp 96–97 °C. Recrystallisation from EtOAc gave an analytical sample: mp 96–97 °C, $[\alpha]_D$ −30.4° (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 5.87 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.83 (ddd, 1 H, $J_{2,3a}$ 6.0, $J_{2,3b}$ 1.0 Hz, H-2), 4.30 (ddd, 1 H, $J_{3a,4}$ 8.0, $J_{3b,4}$ 3.0, $J_{4,5}$ 8.0 Hz, H-4), 3.94 (ddd, 1 H, $J_{5,6a}$ 3.5, $J_{5,6b}$ 5.0 Hz, H-5), 3.81 (dd, 1 H, $J_{6a,6b}$ 12.0 Hz, H-6a), 3.62 (dd, 1 H, H-6b), 2.28 (ddd, 1 H, $J_{3a,3b}$ 14.5 Hz, H-3a), 2.11 (ddd, 1 H, H-3b). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 105.9 (C-1), 80.7 and 80.3 (C-2 and C-4), 72.4 (C-5), 63.0 (C-6), 33.1 (C-3). Anal. Calcd for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.97; H, 8.15.

*6-Azido-3,6-dideoxy-1,2-*O*-isopropylidene-α-*D*-xylo-hexofuranose* (**20**)

*3-Deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-α-*D*-xylo-hexofuranose* (**19**). Regioselective O-tosylation of 3-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (**18**, 550 mg, 2.69 mmol) gave syrupy compound **19** (670 mg, 70%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.76 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.73 (ddd, 1 H, $J_{2,3a}$ 6.0, $J_{2,3b}$ 1.5 Hz, H-2), 4.22 (ddd, 1 H, $J_{3a,4}$ 8.5, $J_{3b,4}$ 3.5, $J_{4,5}$ 6.0 Hz, H-4), 4.07 (two dd, 2 H, $J_{5,6a}$ 7.0, $J_{5,6b}$ 4.0, $J_{6a,6b}$ 12.0 Hz, H-6a, H-6b), 3.93 (dddd, 1 H, $J_{5,OH}$ 4.5 Hz, H-5), 3.01 (d, 1 H, OH), 2.23 (ddd, 1 H, $J_{3a,3b}$ 14.5 Hz, H-3a), 2.05 (ddd, 1 H, H-3b). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 106.0 (C-1), 80.3 and 80.2 (C-2 and C-4), 70.1 (C-5 and C-6), 32.9 (C-3).

*6-Azido-3,6-dideoxy-1,2-*O*-isopropylidene-α-*D*-xylo-hexofuranose* (**20**). Reaction of 3-deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-α-D-*xylo*-hexofuranose (**19**, 1.81 g, 5.05 mmol) with NaN_3, following the general procedure, gave azidodeoxy sugar **20** as a colourless syrup (820 mg, 71%). By addition of EtOAc–hexane, compound **20** crystallised (380 mg, 33%), mp 45–46 °C. Recrystallisation from EtOAc–hexane gave an analytical sample: mp 45–46 °C, $[\alpha]_D$ −34.0° (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.80 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.75 (ddd, 1 H, $J_{2,3a}$ 6.0, $J_{2,3b}$ 1.5 Hz, H-2), 4.18 (ddd, 1 H, $J_{3a,4}$ 8.5, $J_{3b,4}$ 3.0, $J_{4,5}$ 7.5 Hz, H-4), 3.93 (m, 1 H, H-5), 3.37 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 13.0 Hz, H-6a), 3.26 (dd, 1 H, $J_{5,6b}$ 6.0 Hz, H-6b), 2.23 (ddd, 1 H, $J_{3a,3b}$ 14.5 Hz, H-3a), 2.02 (ddd, 1 H, H-3b). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 106.1 (C-1), 81.3 and 80.4 (C-2 and C-4), 71.8 (C-5), 53.0 (C-6), 33.2 (C-3). Anal. Calcd for $C_9H_{15}N_3O_4$: C, 47.16; H, 6.60; N, 18.33. Found: C, 47.44; H, 6.86; N, 18.62.

*6-Azido-3,6-dideoxy-α/β-*D*-xylo-hexose* (**21**). Deprotection of 6-azido-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (**20**, 260 mg, 1.13 mmol) gave a pale-yellow syrup of free aldose **21** (155 mg, 73%), which was purified by chromatography (EtOAc) to furnish a colourless syrup (121 mg, 57%). NMR (D_2O) showed an anomeric mixture of furanose and pyranose forms. ^{13}C NMR (D_2O, 50.3 MHz): δ 104.7 (C-1, β-furanose), 100.7 (C-1, β-furanose), 97.5 (C-1, β-pyranose), 96.1 (C-1, α-pyranose).

*3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-*L*-xylo-hexofuranose* (**23**).—Reduction and protection of 3-deoxy-L-*xylo*-hexono-1,4-lactone (**22**, 5.80 g, 35.8 mmol), according to the general procedures given above, yielded a crystalline residue (3.15 g, 36%). By addition of hexane, deoxy sugar **23** crystallised (1.31 g, 15%), mp 73–76 °C. Several recrystallisations from hexane afforded an analytical sample: mp 76–77.5 °C, $[\alpha]_D$ +29.3° (*c* 1.0, $CHCl_3$). NMR data as for the D-*xylo* isomer **17**. Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.26. Found: C, 58.74; H, 7.96.

*3-Deoxy-1,2-*O*-isopropylidene-α-*L*-xylo-hexofuranose* (**24**).—Regioselective deprotection of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-

L-*xylo*-hexofuranose (**23**, 3.20 g, 13.1 mmol) gave a yellow syrup that was purified by chromatography (EtOAc) to give crude compound **24** (1.10 g, 41%). By addition of Et_2O, **24** crystallised (544 mg, 20%), mp 95–97 °C. Recrystallisation from EtOAc–Et_2O gave an analytical sample: mp 96–97 °C, $[\alpha]_D$ +30.6° (*c* 1.0, $CHCl_3$). NMR data were identical with values for the D-*xylo* isomer **18**. Anal. Calcd for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.95; H, 7.67.

3-Deoxy-1,2-O-*isopropylidene-6*-O-*tosyl*-α-L-xylo-*hexofuranose* (**25**).—Regioselective O-tosylation of 3-deoxy-1,2-*O*-isopropylidene-α-L-*xylo*-hexofuranose (**24**, 0.93 g, 4.55 mmol) gave sulfonate **25** as a syrup (1.63 g, quant). NMR data were identical with those for the D-*xylo* isomer **19**.

6-Azido-3,6-dideoxy-1,2-O-*isopropylidene*-α-L-xylo-*hexofuranose* (**26**).—Reaction of 3-deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-α-L-*xylo*-hexofuranose (**25**, 1.57 g, 4.38 mmol) with NaN_3 gave product **26** (680 mg, 68%) as a syrup. By addition of EtOAc–hexane, compound **26** crystallised (320 mg, 32%), mp 45–46 °C. Recrystallisation from EtOAc–hexane afforded an analytical sample: mp 45–46 °C, $[\alpha]_D$ +34.3° (*c* 0.9, $CHCl_3$). NMR data were identical with those for the D-*xylo* isomer **20**.

6-Azido-3,6-dideoxy-α/β-L-xylo-*hexose* (**27**). —Deprotection of 6-azido-3,6-dideoxy-1,2-*O*-isopropylidene-α-L-*xylo*-hexofuranose (**26**, 400 mg, 1.75 mmol) gave compound **27** (270 mg, 82%) as a pale-yellow syrup. NMR data were identical with those for the D-*xylo* isomer **21**.

1,3,6-Trideoxy-1,6-imino-D-ribo-*hexitol* (**28**).—Hydrogenation of 6-azido-3,6-dideoxy-α,β-D-*ribo*-hexose (**9**, 93 mg, 0.49 mmol) gave compound **28** (72 mg, 100%) as a pale-yellow syrup. Purification by chromatography (5% NH_3 in 1:1 MeOH–CH_2Cl_2) yielded an analytical sample. ^{1}H NMR (MeOH-d_4, 250 MHz): δ 3.8–3.9 (complex, 3 H, H-2, H-4, H-5), 2.97 (dd, 1 H, *J* 4.5, *J* 14.0 Hz, H-6 or H-1), 2.88 (complex, 2 H, H-1 and/or H-6), 2.80 (dd, 1 H, *J* 6.5, *J* 14.0 Hz, H-6 or H-1), 2.17 (ddd, 1 H, $J_{3a,3b}$ 14.0, *J* 8.5, *J* 10.0 Hz, H-3a), 1.93 (ddd, 1 H, *J* 4.0, *J* 4.0 Hz, H-3b). ^{13}C NMR (MeOH-d_4, 62.9 MHz): δ 73.9 (C-5), 71.6 (C-4), 68.7 (C-2), 56.0 (C-6), 52.2 (C-1), 38.8 (C-3). HRFABMS. Calcd for $C_6H_{14}NO_3$: 148.0974. Found: $[M+H]^+$ 148.0979.

1,3,6-Trideoxy-1,6-imino-D-arabino-*hexitol* (**29**).—Hydrogenation of 6-azido-3,6-dideoxy-α,β-D-*arabino*-hexose (**15**, 97 mg, 0.51 mmol) gave product **29** (63 mg, 84%) as a pale-yellow syrup. Purification by chromatography (5% NH_3 in 1:1 MeOH–CH_2Cl_2) furnished an analytical sample. ^{1}H NMR (MeOH-d_4, 250 MHz): δ 4.08 (ddd, 1 H, $J_{3a,4}$ 9.5, $J_{3b,4}$ 2.5, $J_{4,5}$ 2.5 Hz, H-4), 4.01 (dddd, 1 H, $J_{1a,2}$ 4.5, $J_{1b,2}$ 6.0, $J_{2,3a}$ 4.5, $J_{2,3b}$ 6.0 Hz, H-2), 3.85 (ddd, 1 H, $J_{5,6a}$ 4.0, $J_{5,6b}$ 6.0 Hz, H-5), 3.10 (dd, 1 H, $J_{1a,1b}$ 14.0 Hz, H-1a), 2.95 (dd, 1 H, $J_{6a,6b}$ 14.0 Hz, H-6a), 2.86 (dd, 1 H, H-6b), 2.73 (dd, 1 H, H-1b), 2.29 (ddd, 1 H, $J_{3a,3b}$ 14.5 Hz, H-3a), 1.75 (ddd, 1 H, H-3b). ^{13}C NMR (MeOH-d_4, 62.9 MHz): δ 74.6 (C-5), 70.4 (C-4), 67.8 (C-2), 55.5 (C-6), 52.1 (C-1), 38.1 (C-3). HRFABMS. Calcd for $C_6H_{14}NO_3$: 148.0974. Found: $[M+H]^+$ 148.0959.

1,3,6-Trideoxy-1,6-imino-D-xylo-*hexitol* (**30**).—Hydrogenation of 6-azido-3,6-dideoxy-α,β-D-*xylo*-hexose (**21**, 46 mg, 0.24 mmol) gave a pale-yellow syrup of imino alditol **30** (30 mg, 85%). Purification by chromatography (5% NH_3 in 1:1 MeOH–CH_2Cl_2) gave an analytical sample. ^{1}H NMR (MeOH-d_4, 250 MHz): δ 4.01 (dddd, 1 H, $J_{1a,2}$ 5.0, $J_{1b,2}$ 6.5, $J_{2,3a}$ 6.5, $J_{2,3b}$ 3.5 Hz, H-2), 3.87 (ddd, 1 H, $J_{3a,4}$ 3.0, $J_{3b,4}$ 8.0, $J_{4,5}$ 6.5 Hz, H-4), 3.55 (ddd, 1 H, $J_{5,6a}$ 4.0, $J_{5,6b}$ 6.5 Hz, H-5), 3.05 (dd, 1 H, $J_{1a,1b}$ 14.0 Hz, H-1a), 3.05 (dd, 1 H, $J_{6a,6b}$ 14.0 Hz, H-6a), 2.74 (dd, 1 H, H-6b), 2.65 (dd, 1 H, H-1b), 2.05 (ddd, 1 H, $J_{3a,3b}$ 14.5 Hz, H-3a), 1.95 (ddd, 1 H, H-3b). ^{13}C NMR (MeOH-d_4, 62.9 MHz): δ 76.6 (C-5), 71.5 (C-4), 67.6 (C-2), 56.4 (C-6), 52.9 (C-1), 39.9 (C-3). HRFABMS: Calcd for $C_6H_{14}NO_3$: 148.0974. Found: $[M+H]^+$ 148.0974.

1,3,6-Trideoxy-1,6-imino-L-xylo-*hexitol* (**31**).—Hydrogenation of 6-azido-3,6-dideoxy-α,β-L-*xylo*-hexose (**27**, 130 mg, 0.67 mmol) gave a pale-yellow syrup of product **31** (54 mg, 55%). Purification by chromatography (5% NH_3 in 1:1 MeOH–CH_2Cl_2) gave an analytical sample. NMR data as for enantiomer **30**. HRFABMS: Calcd for $C_6H_{14}NO_3$: 148.0974. Found: $[M+H]^+$ 148.0972.

1,2,6-Trideoxy-1,6-imino-D-arabino-*hexitol* (**33**).—6-Amino-2,6-dideoxy-D-*arabino*-hexonolactam (**32**, 1.0 g, 6.2 mmol) was suspended in CH_3CN (10 mL), and a mixture of hexamethyldisilazane (4.30 mL, 19.6 mmol) and chlorotrimethylsilane (0.17 mL, 0.10 mmol) was added. After stirring at 80 °C for 1 h, the mixture was filtered, and the filtrate was concentrated to a syrup. The residue was dissolved dioxane (35 mL), and under an atmosphere of N_2 $BH_3{\cdot}Me_2S$ (10 M, 3.1 mL, 31 mmol) was added. The mixture was then stirred for 5 h at 100 °C and allowed to stand at ambient temperature overnight. Hydrochloric acid (1 M, 26 mL) was added, and the mixture was kept under reflux for 1 h, filtered, concentrated, and co-concentrated with 1% v/v acetyl chloride–MeOH (3 ×) to yield a crude residue (1.13 g, >100%). Purification by chromatography (5% NH_3 in 1:1 MeOH–CH_2Cl_2) gave an analytical sample. ^{1}H NMR (MeOH-d_4, 250 MHz): δ 3.94 (ddd, 1 H, $J_{4,5}$ 2.5, $J_{5,6a}$ 6.5, $J_{5,6b}$ 2.5 Hz, H-5), 3.82 (ddd, 1 H, $J_{2a,3}$ 3.0, $J_{2b,3}$ 7.5, $J_{3,4}$ 7.5 Hz, H-3), 3.60 (dd, 1 H, H-4), 2.95 (dd, 1 H, $J_{6a,6b}$ 14.0 Hz, H-6a), 2.88 (complex, 2 H, H-1a and H-1b), 2.83 (dd, 1 H, H-6b), 1.98 (dddd, 1 H, $J_{1,2a}$ 4.5 and 6.0, $J_{2a,2b}$ 15.0 Hz, H-2a), 1.72 (dddd, 1 H, $J_{1,2b}$ 6.0 and 8.0 Hz, H-2b). ^{13}C NMR (MeOH-d_4, 62.9 MHz): δ 9.3 (C-4), 71.6 and 71.4 (C-3 and C-5), 48.7 (C-6), 43.5 (C-1), 34.2 (C-2). HRFABMS: Calcd for $C_6H_{14}NO_3$: 148.0974. Found: $[M+H]^+$ 148.0960.

6-Azido-3,6-dideoxy-α/β-D-erythro-*hex-2-ulose* (**34**).—A solution of 6-azido-3,6-dideoxy-α,β-D-*ribo*-hexose (**9**, 110 mg, 0.58 mmol), water (1 mL) and 1% aq $MgSO_4$ (one drop) was adjusted to pH 8.5 by the addition of solid Na_2CO_3. Sweetzyme T (immobilised glucose isomerase EC. 5.3.1.5, 110 mg) was added, and the mixture was stirred at 40 °C for 3 days. The brown residue was filtered and concentrated to a pale-yellow syrup (130 mg) that was purified by chromatography (EtOAc) to give a 1:9 mixture of **9** and **34** (110 mg) as a clear syrup. This mixture (100 mg, 0.54 mmol) was dissolved in water (8.5 mL) and $BaCO_3$ (380 mg) and Br_2 (180 mg, 1.1 mmol) were added. After 20 min, air was bubbled through the mixture to remove excess Br_2. Filtration and concentration gave a colourless foam that was purified by chromatography to give ketose **34** (64 mg, 70% overall). From ^{1}H NMR spectra (MeOH-d_4) a mixture of furanose forms and the open-chain ketose were identified.

1,4,5-Trideoxy-1,5-imino-D-lyxo-*hexitol* (**35**).—Hydrogenation of 6-azido-3,6-dideoxy-α,β-D-*erythro*-hex-2-ulose (**34**, 64 mg, 0.34 mmol) gave a pale-yellow syrup (52 mg, 100%) that could be crystallised from acetone to give imino alditol **35** (19 mg, 37%), mp 140–150 °C, $[\alpha]_D$ −29.1° (*c* 1.6, MeOH). ^{1}H NMR (MeOH-d_4, 250 MHz): δ 3.74 (ddd, 1 H, $J_{1a,2}$ 3.0, $J_{1b,2}$ 1.5, $J_{2,3}$ 3.0 Hz, H-2), 3.66 (ddd, 1 H, $J_{3,4a}$ 6.0, $J_{3,4b}$ 11.0 Hz, H-3), 3.55 (dd, 1 H, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 13.5 Hz, H-6a), 3.51 (dd, 1 H, $J_{5,6b}$ 5.0 Hz, H-6b), 3.06 (dd, 1 H, $J_{1a,1b}$ 13.5 Hz, H-1a), 2.70 (dd, 1 H, H-1b), 2.60 (ddd, 1 H, $J_{4a,5}$ 5.0 Hz, H-5), 1.65 (complex, 1 H, H-4a), 1.56 (dd, 1 H, $J_{4a,4b}$ 12.5 Hz, H-4b). ^{13}C NMR (MeOH-d_4, 62.9 MHz): δ 71.0 (C-2), 68.6 (C-3), 66.0 (C-6), 57.7 (C-5), 50.8 (C-1), 32.2 (C-4). HRFABMS: Calcd for $C_6H_{14}NO_3$: 148.0974. Found: $[M+H]^+$ 148.0960.

Inhibition studies. α-D-Glucosidase from baker's yeast, β-D-glucosidase from almonds, α-D-galactosidase from green coffee beans, β-D-galactosidase from *Escherichia coli*, α-D-mannosidase from jack bean, β-D-mannosidase from snail acetone powder, β-*N*-acetylglucosaminidase from jack beans and α-L-fucosidase from bovine kidney were purchased from Sigma Chemical Co. K_i determinations were performed at 25 °C for α-D-galactosidase, β-D-galactosidase, α-D-mannosidase and at 35 °C for α-D-glucosidase, β-D-glucosidase, β-D-mannosidase, α-L-fucosidase, β-*N*-acetylglucosaminidase using the corresponding *p*-nitrophenyl-α-(or β)-glycoside at various final concentrations ranging from 0.7×10^{-3} to 2.7×10^{-3} mol L^{-1} (for β-*N*-acetylglucosaminidase: 0.16×10^{-3} to 0.66×10^{-3} mol L^{-1}) at pH 6.8 (0.12 mol L^{-1} phosphate buffer). For the inhibition studies, inhibitors were incorporated into the buffer to give a final concentration of 1.7×10^{-5} mol L^{-1}. The enzymes were incorporated into the buffer to give a final concentration of 0.17 units/mL. Dissociation constants for

inhibition were calculated from a Hanes plot ($[S]/v$ against $[S]$) from the rates of substrate hydrolysis in the absence and presence of inhibitor.

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